

## REMARKS/ARGUMENT

Claims 13-23 from the original patent and new claims 24-44 are now pending. Claims 1-12 have been canceled without prejudice. New claims 24-44 have been added. Claims 13, 14, 15, 16, 17, 19 and 20 were the subject of a preliminary amendment, and claims 13, 15, 22 and 23 are amended by the present amendment. Support, for the amendments and new claims, is found in the original patent as set forth in attached Appendix A. It is urged that the new claim set, following entry of this Amendment, sets forth subject matter that is neither disclosed nor suggested by the prior art.

The Examiner is thanked for clearly setting forth the remaining issues to be addressed, especially at pages 7-8 of the Office Action concerning issues that the Examiner believes not to have been overcome by Applicant's August 11, 2005 response.

Specifically, the Examiner states at page 7 of the Office Action that Applicant's 2005 proof showing that various important parameters (e.g. citric acid concentration, pH, etc.) were outside of the state of numerical ranges in the claims, did not sufficiently distinguish the claims because many of the claims use the word "about" as a modifier to the stated numerical ranges. In response, Applicant has removed the word "about" from independent claims 13, 15, 22 and 23, and thus from claims that depend therefrom. In view of these amendments, the stated ranges for the parameters cited in the claims are precise and the prior art is not within these ranges for the reasons stated in the Stern Declaration and response submitted in August 2005.

The Examiner also states at page 7 of the Office Action that the Markush language utilized in the claims (prior to the present amendment) would have covered a mixture of citric acid and citric acid salt that, in the aggregate, was too high to be within the stated concentration limits, based on an individual component (e.g. citric acid alone) being within the stated range. In response, Applicant has amended the Markush language in claims 13 and 15 (and by implication all claims dependent therefrom) to specifically recite that it is the aggregate concentration that controls. This is accomplished by the following language that exists following entry of the present amendment:

"a bioavailability enhancing agent selected from the group consisting of citric acid, citric acid salt and a combination thereof, wherein the aggregate concentration of all such bioavailability enhancing agents is . . ." (emphasis added)

This is not believed to be a substantive change from the prior Markush language (“a [stated] concentration of a component selected from the group consisting of citric acid, citric acid salt and a combination thereof . . .”). In the pre-amendment Markush language, because “combination” is specifically recited, it is implied that “citric acid” means citric acid alone (without citric acid salt), and conversely that “citric acid salt” means citric acid salt alone (without citric acid). Otherwise the recitation of a “combination” would have been redundant. Nonetheless, it is urged that the new language inserted by the present amendment clarifies any ambiguity may have concerned the Examiner regarding the pre-amendment language, and makes totally clear that it is the aggregate concentration (whether derived from citric acid alone, citric acid salt alone, or a combination of both) that must fall within the stated mathematical ranges.

With the mathematical ranges recited in the claims now defined with precision for the reasons stated above. The Stern Declaration filed in August 2005 establishes that the cited prior art did not provide pharmaceutical products having the mathematical limitations of the claims. See especially page 4 of the Stern Declaration summarizing the mathematical values in table form. These strict mathematical limitations are critical to the performance of the product as illustrated in Tables 1 and 3. The prior art’s failure to disclose or suggest these critical ranges is fatal to the art rejections. Broad generic ranges, for example the pH 3-8 or citric acid range from 0.01-0.5 M that the examiner alleges for the Grebow reference (Office Action at 2), cannot anticipate claims to narrow specific ranges that applicant has proven critical. Metabolite Laboratories, Inc v. Laboratory Corporation of America Holdings, 370 F.3d 1354, 1367 (Fed. Cir. 2004) (“A prior art reference that discloses a genus still does not inherently disclose all species within that broad category”). For all of the foregoing reasons, and for the reasons stated in the Stern Declaration and the accompanying response submitted in August 2005, it is urged that the art rejections of the product claims (and claims dependent therefrom) should be withdrawn.

Regarding method claims 22 and 23 (and claims dependent therefrom), citric acid is specifically utilized for the purpose of improving stability or bioavailability. These represent new uses of an old compound, patentable as uses under a long line of precedents. As the U.S. Court of

Appeals for the Federal Circuit stated in In re King, 801 F.2d 1324, 1326 (1986) (emphasis added):

“Under the principles of inherency, if a structure in the prior art necessarily functions in accordance with the limitations of a process or method claim of an application, the claim is anticipated. This is not to say that the discovery of a new use for an old structure based on unknown principles of the structure might not be patentable to the discoverer as a process. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957).”

The method claims of the present application represent a classic example of a new use of an old compound - - citric acid. It is applicant, who for the first time, has discovered the stability and bioavailability enhancement that can be provided by using citric acid (or its salt) within the stated range. The Examiner notes at page 8 of the Office Action that prior art formulations would have sought stability and bioavailability. The prior art, however, does not disclose or suggest that those desirable qualities may be accomplished with citric acid (or its salt) as taught by applicant. Accordingly, it is urged that the art rejections of method claims 22, 23 (and claims dependent therefrom) should also be withdrawn.

It is believed that the application is now in condition for allowance.

EXPRESS MAIL CERTIFICATION

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail Label No. EV606197832US in an envelope addressed to: Mail Stop Reissue, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 21, 2006

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Date of Signature

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Respectfully submitted,

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## APPENDIX A

Claim Number (Status)	Nature of Change/Recitation	Supporting Text in Original Patent
1-12 (canceled)	n/a	n/a
13 (pending)	citric acid concentration; rewritten in independent form; “and/or” changed to Markush format	Table 1; Table 3
14 (pending)	claim dependency only	original claim 14
15 (pending)	rewritten in independent format; “and/or changed to Markush format; no substantive change	original claim 15
16 (pending)	claim dependency only	original claim 16
17 (pending)	claim dependency only	original claim 17
18 (pending)	no change	original claim 18
19 (pending)	typographical error “MRC”; no substantive change	original claim 19
20 (pending)	claim dependency only	original claim 20
21 (pending)	no change	original claim 21
22 (pending)	“about” removed	original claim 22
23 (pending)	“about” removed	original claim 23
24 (pending)	citric acid concentration	Table 1; Table 3
25 (pending)	pH range	col. 3, line 12
26 (pending)	pH range	col. 3, line 12
27 (pending)	aqueous saline	col. 3, line 2
28 (pending)	viscosity	col. 3, lines 19-20
29 (pending)	polyoxyethylene (20) sorbitan monooleate	original claim 16
30 (pending)	preservatives	original claim 17

Claim Number (Status)	Nature of Change/Recitation	Supporting Text in Original Patent
31 (pending)	aqueous saline; osmotic pressure	col. 3, line 2; col. 3, lines 16-18
32 (pending)	salmon calcitonin	examples 1, 2 and 3
33 (pending)	salmon calcitonin	examples 1, 2 and 3
34 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
35 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
36 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
37 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
38 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
39 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
40 (pending)	method of nasal administration	original claim 20; col. 3, lines 43-56
41 (pending)	pH range; citric acid concentration	col. 3, line 12; Tables 1 and 3
42 (pending)	pH range; citric acid concentration	col. 3, line 12; Tables 1 and 3
43 (pending)	aqueous saline; osmotic pressure	col. 3, line 2; col. 3, lines 16-18
44 (pending)	aqueous saline; osmotic pressure	col. 3, line 2; col. 3, lines 16-18